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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,221	12/13/2001	Nathan S. Lewis	CIT1300-1	9894

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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 05/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,221	LEWIS ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicants' arguments filed March 01, 2005 have been fully considered but they are not persuasive. Applicant's arguments in the Preliminary Amendment of March 01, 2005 from page 6, line 11 ("Applicants have demonstrated ...") to page 9, line 14 ("... acids, nucleic acid, lipid, and the like.") appear to be verbatim the same as the arguments set forth in Response of January 31, 2005 from page 7, line 4 ("Applicants have demonstrated ...") to page10, line 6 ("... acids, nucleic acid, lipid, and the like."). These arguments address whether the range of analytes for the claimed analyte screening system is enabled (scope of enablement). The Preliminary Amendment of March 01, 2005 from page 9, line 15 to page 11, line 3 addresses whether the range of sensor types is enabled. The remainder of the Preliminary Amendment of March 01, 2005 (page 11, from the second paragraph to the last paragraph) addresses the rejection of claims 3-8 for not being enabled and rely on the first set of arguments noted above.

As for enablement of analytes, Applicants assert

> Each of the foregoing tested analytes [alcohols, halogenated hydrocarbons, aromatics, unsubstituted hydrocarbons, and esters] is characteristic of most if not all side groups present in organic molecules including amino acids (building blocks of proteins and enzymes), nucleic acids (building blocks of DNA/RNA), lipids (e.g., hormones) and the like. *Page 6 of Preliminary Amendment of March 01, 2005*

Indeed, but behold the vast differences in specific activity, chemical or physical property, or function of proteins, enzymes, lipids (e.g. hormones), and nucleic acids (DNA/RNA) even though they may have some of the same side groups. Applicants are commiting the fallacies of composition and false analogy. Applicants believe that what is true of the parts will be true of any combination of the parts and that because two objects have some similarities in unimportant ways they will be similar in important ways. One with ordinary skill in the art would not expect arbitrary arrangements of side groups on some molecular core or backbone to result in molecules with similar activities, chemical or physical properties or functions. A single change in a base-pair in a DNA molecule can result in a missense mutation, in which an amino acid in the corresponding protein (gene product) also changes or a nonsense mutation, in which the resulting polypeptide chain ends prematurely at the at point. These mutated proteins can reduce the activity of the proteins or even cause cancer or genetic defects.[1] Applicants seem to believe that if two molecules have some of the same side groups that they will have similar activities, chemical or physical properties or functions. This is oversimplified as the similarity of activities, chemical or physical properties or functions will depend on how many side chains are the same, whether the corresponding locations of the side chains are the same, and whether any side chain predominates over the others and the relevance of these side chains to the activity, chemical or physical property, or function being predicted.

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[1] Unit II:Genes, Information, and Heredity from 11th Hour Study Tips: Introduction to Biology. Downloaded from www.blackwellpublishing.com/11thhour/wilson/about/u2ch10.html on May 05, 2005.

In a similar manner Applicants assert

> The Office Action states, for example, that lipids and fatty acids have some similarities to alcohols but allegedly would not be expected to have the same chemical properties because of different functionalities. Applicants fail to see the reasoning in this statement. Lipids and fatty acids (e.g., hormones) not only have some resemblance to alcohols, but they are also long chain hydrocarbons. [emphasis added] *Page 8 of Preliminary Amendment of March 01, 2005*

Does this mean that in Applicants' view "alcohol", "fatty acids," and "long chain hydrocarbons" are synonyms? Applicants seem to blur the distinction between various types of molecules. The categories "lipids", "alcohols", and "long chain hydrocarbons" designate not only different structures, but also different activities.

As for enablement of different types of sensor arrays, Applicants believe that results obtained with one type of sensor array will be duplicated with any other type of sensor array that has at least one shared feature with the first type of sensor array. In particular, Applicants assert

> If one were to use the same collection of polymers demonstrated to work in Sisk and Lewis, but transduce the signal using optical or mechanical transducers instead of electrical transduction, a signal profile would be obtained upon contact with an analyte. After all, only the transducers differ in what physical type of signal they deliver .... *Page 9 of Preliminary Amendment of March 01, 2005* continued onto page 10

Applicants again commit the fallacy of false analogy. US 6,846,638 B2 and US 6,839,636 were cited by Applicants as example sensors on *Page 6 of Preliminary Amendment of March 01, 2005.* '638 and '636 disclose sensors for identifying and quantifying analytes that use a database of stored signal patterns by looking for a matching pattern. See col. 1:10-17 and col. 34:7-17 in '638 and col. 15:17-53 in '636. In stark contrast, claim 1 requires the computer to be "operative to compare the sensor

array signal profiles to the plurality of previously obtained signal profiles from the plurality of standard samples not including the analyte of interest, wherein the comparison of the sensor array signal profiles of the previously obtained signal profiles is indicative of a specific activity, chemical or physical property, or function of the analyte of interest. [emphasis added]." Just because some types of information such as identification and quantity of an analyte can be derived from a transducer signal array does not mean that any type of information, such as specific activity, chemical or physical property, or function of the analyte of interest can be derived from the same transducer signals. Indeed, even for the same types of information sought such as identification and quantity of an analyte '638 and '636 both recognize that some transducers may be more suitable than others depending on the analyte and that substantial changes in the structure and composition of the active sensor areas may be needed for the same analyte analyzed with different transducers. See in '638 col. 30:26-34; col. 32:31-39; and col. 40:33-62 and in '636 see col. 13:56 – col. 14:15. In light of the passage quoted above from Applicants' Preliminary Amendment it is noteworthy that '636' states "... particular analytes are more responsive to particular polymer types e.g., ammonia and methanol are responsive to polypyrrole. In addition, combustible gas analytes are easily detected with metal oxide sensors." See col. 14:11-15. Thus the reference cited by Applicants cast a doubt on whether a polymer used in one type of transducer can be placed in another type of transducer to obtain the same results as obtained with the first type of transducer. Finally, success at matching a measured transducer array signal with a stored transducer signal array does not

indicate further potential success at determining a property of an unknown analyte from which no transducer signal array has been stored.

Applicants also commit the fallacy of equivocation. A "transducer" is not a "detector" or "sensor." It is one thing to measure a property of something by measuring a signal emitted or affected by that thing, which a detector or sensor does. It is quite another thing to change the measured signal from one form to another, which a transducer does. Applicants assert

> After all, only the transducers differ in what physical type of signal they deliver, but are trandsucing the same fundamental pattern of responses from the same collection of materials to the same analyte. In other words, the polymers themselves would be interacting with the analyte in a similar fashion, but the transducer would be merely optical or mechanical compared to electrical. *Page 10 of Preliminary Amendment of March 01, 2005*

While the "polymers may be interacting with the analyte in a similar fashion" in an optical sensor, a mechanical sensor, and an electrical sensor, this does not mean that any change resulting in the polymer from interacting with the analyte can be detected by these sensors as they each *measure a different property* of the polymer, such as light absorbance or transmittance; stress or strain; or resistance, conductivity, current. Are Applicants asserting that merely by using the same polymer used in an array of electrical resistances for predicting the inhibitory activity of gaseous alcohols on cytochrome P-450 aniline hydroxylation instead in an optical, mechanical, or magnetic sensor array of choice the optical, mechanical, or magnetic sensor array so modified will then be able to predict the inhibitory activity of gaseous alcohols on cytochrome P-450 aniline hydroxylation?

As stated by the Examiner in the Advisory action of February 15, 2005

> Applicants have not demonstrated a reasonable physical or chemical correlation between alcohols and other classes of analytes, such as, hormones, nucleic acids, polypeptides, antibodies, enzymes, or carbohydrates. Nor have Applicants shown how predicting the inhibitory activity of gaseous alcohols on cytochrome P-450 aniline p-hydroxylation using an array of electrical resistances establishes the predictability of enzymatic activity using an array of optical and magnetic sensors. Although Applicants have, in the Sisk article, tested and demonstrated their invention for at least seventy-five species, these species do not bear any apparent kinship to hormones, nucleic acids, polypeptides, antibodies, enzymes, or carbohydrates. Likening an amino acid to a hydrocarbon alkane or a hydrocarbon aromatic just because the amino acid has an alkane or aromatic side chain is a significant blurring or extending of what one with ordinary skill in the art would understand an amino acid to be.

For these reasons and the reasons set forth in the rejections under 35 U.S.C. 112, first paragraph, the Examiner has not been persuaded that claims 1, 2, and 9-15 do not exceed the scope of enablement and that claims 3-8 are enabled.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 2, and 9-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for predicting the inhibitory action of alcohols on cytochrome P-450 aniline p-hydroxylation and perhaps some other properties of alcohols or simple organic molecules, such as vapor pressure, does not reasonably provide enablement for predicting or determining the specific activity, chemical or

physical property, or function of compounds other than alcohols. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant claims a device that can predict or determine the specific activity, chemical or physical property, or function of an unknown analyte by comparing its signal profile from a sensor array to a collection of sensor array signal profiles from other substances.

Claim 1 is unbounded in terms of what the analyte can be and what specific activity, chemical or physical property, or function can be determined or predicted. That Applicant intends for an almost unlimited scope can be seen from claims 4, 5, and 8. Claim 4, for example, states that the analyte can be a lipid, a hormone, a fatty acid, a nucleic acid, a polypeptide, or a carbohydrate. Claim 5, further states that the analyte can be an antibody, an enzyme, or a protein. Claim 8 states that the specific activity of an enzyme analyte that can be predicted or determined is a binding activity, an inhibitory activity, and a modulating activity.

Claim 1 is also unbounded as to the type of sensor array. Claim 11 states that the sensors may change optically, electrically, magnetically, mechanically, physically, or a combination thereof.

The invention of claims 1, 2, and 9-15 is of a complex nature as it uses a computer-supported system not to identify or quantitate, but to determine specific activities, chemical or physical properties, or functions of an unlimited scope of analytes including enzymes and nucleic acids with any type of sensor array.

A review of related work in the field shows that others have limited themselves to more modest goals of predicting a particular property on a select type of analyte, such as monitoring sausage fermentation[2], predicting gasoline properties[3], or discriminating chirality with simple gas sensors[4].

The specific activities, chemical or physical properties, or functions of analytes such as antibodies, enzymes, proteins and nucleic acids are rarely predictable. If otherwise, there would be no need for the many hundreds of journal articles on these substances written in dozens of biochemical and chemical journals each year. Old Yellow Enzyme, an arbitrary choice, is illustrative. Although it had been discovered and purified almost 60 years before the time of the invention of the claimed invention and much research had been done on this substance it was only in the few years prior to the invention of the claimed invention that the enzymatic properties and structure-function relations were better understood. Its physiologic role is still unknown. See the Coordinating Editor's comment and the abstract in "Flavoprotein Structure and Mechanism 8 – Structure-function relations for old yellow enzyme" by Karplus et al. The FASEB Journal, vol. 9, December 1995.

Applicant's only example in his disclosure is predicting "the inhibitory action of a series of alcohols on cytrochrome P-450 aniline p-hydroxylation" (described on pages 22-35 of the specification). This involves passing gas phase alcohols over the sensor array to "train" it with alcohols used as standards and to test the sensor array with

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[2] Ekov et al. « Monitoring sausage fermentation using an electronic nose, » Journal of the Science of Food and Agriculture (1998), 76(4), 525-532.
[3] Litani-Barzlai et al. « Online remote prediction of gasoline properties by combined optical methods, » Analytica Chimica Acta (1997), 339(1-2), 193-199.

unknown alcohols. With only this example as guidance one with ordinary skill in the art would not be able to use Applicant's invention to predict the specific activity, a binding activity, an inhibitory activity, or a modulating activity of an enzyme, let alone predict the secondary, tertiary, or quaternary structures of proteins, or predict the functions of various antibodies or antigens or RNA or DNA sequences, without undue experimentation, if such predictions could be made at all using a sensor array response profile. Should enzymes, proteins, and nucleic acids be also put into the gas phase and passed over the same array of sensors? How is one with ordinary skill in the art to select the right sensor for the unknown analyte of interest and the specific activity, chemical or physical property, or function of the analtye to be predicted? Can crystalline colloidal array sensors and capacitance sensors (claim 12) be used for enzymes and antibodies? Can these sensors be used to determine any specific activity, chemical or physical property, or function of enzymes and antibodies? How is a magnetic sensor array to be used to predict the inhibitory action of alcohols on cytochrome P-450 aniline p-hydroxylation?

Thus, the scope of claims 1, 2, and 9-15 is too broad because of the almost unlimited scope of the claims in terms of analyte and analyte property, the state of the art and relative skill in the art at the time of invention, the limited guidance and example provided by Applicant's disclosure, the unpredictability of properties of various proteins, enzymes, antibodies, DNA and RNA, and the undue experimentation required to use the analyte screening system.

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[4] Bodenh ̄er et al., « Chiral discrimination by Simple Gas sensors, » Transducers '97, June 16-19, 1997

4. Claims 3-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As discussed in the rejection of claims 1, 2, and 9-15 are rejected under 35 U.S.C. 112, first paragraph, with the only disclosed guidance and example being predicting the inhibitory action of alcohols on cytochrome P-450 aniline p-hydroxylation from a sensor array response profile to a gas phase sample of alcohols, one with ordinary skill in the art would not be able to use Applicant's invention to predict the specific activity, a binding activity, an inhibitory activity, or a modulating activity of an enzyme, let alone predict the secondary, tertiary, or quaternary structures of proteins, or predict the function of various antibodies or antigens or RNA or DNA sequences, without undue experimentation, if such predictions could be made at all.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753
May 5, 2005